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EXAMINER	
HARRIS, ALANA M	
ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
12/03/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/535,156	NEPVEU ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-28* is/are pending in the application.

4a) Of the above claim(s) *21-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/21/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment and Arguments

1. Claims 11-28 are pending.

Claims 21-25, drawn to non-elected inventions are withdrawn from examination.

Claims 1-10 have been cancelled.

Claims 11-28 have been added.

Claims 11-20 and 26-28, to the extent protein is detected is examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections

Claim Objections

3. The objection of claim 4 because of the following informality: it includes non-elected subject matter, a method reading on the detection of nucleic acids has been withdrawn in light of the cancellation of the claim.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

4. The rejection of claims 1-5 and 10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of Applicants' cancellation of the claims.

5. The rejection of claims 1-5 and 10 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting the presence or absence of CDP/Cux isoforms comprising contacting a sample with an antibody, which specifically recognizes a truncated CDP/Cux isoform, does not reasonably provide enablement for diagnosing or staging cancer comprising detecting the level of a truncated CDP-Cux isoform is withdrawn in light of Applicants' cancellation of the claims.

6. The rejection of claims 1-5 and 10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the cancellation of the claims.

Claim Rejections - 35 USC § 102

7. The rejection of claims 1-3 and 5 under 35 U.S.C. 102(b) as being anticipated by Moon et al. (Molecular and Cellular Biology 21(18): 6332-6345, September 2001/ IDS reference C43 submitted April 5, 2006) as evidenced by Goulet (Biol. Chem. 387: 1285-1293, September 2006) is withdrawn in light of the cancellation of the claims.

8. The rejection of claims 1-3 and 5 under 35 U.S.C. 102(a) as being anticipated by Moon et al. (Int. J. Cancer 100: 429-432, August 2002) is withdrawn in light of the cancellation of the claims.

Claim Rejections - 35 USC § 103

9. The rejection of claims 1-3, 5 and 10 under 35 U.S.C. 103(a) as being unpatentable over Moon et al. (Molecular and Cellular Biology 21(18): 6332-6345, September 2001/ IDS reference C43 submitted April 5, 2006) is withdrawn in light of Applicants' cancellation of the claims.

10. The rejection of claims 1-3, 5 and 10 under 35 U.S.C. 103(a) as being unpatentable over Moon et al. (Int. J. Cancer 100: 429-432, August 2002) is withdrawn in light of Applicants' cancellation of the claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 11-20 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

THIS IS A NEW MATTER REJECTION.

Applicants have added new claims for examination, which recite for example,

> "**11. (New) A method of detecting a level of an amino-terminally truncated CDP/Cux polypeptide variant in a sample wherein said polypeptide variant is:**
>
> **a) a variant which is encoded by a nucleic acid produced from transcriptional initiation within intron 20 of the CDP/Cux locus;**
>
> **b) a variant which is encoded by a CDP/Cux mRNA comprising a translation start site within exon 21;**
>
> **c) a variant which lacks Cut repeat domains CR1 and CR2;**
> **d) a variant which contains only two DNA binding domains; or**
> **e) any combination of a)-d).** "

Applicants note in their Remarks filed August 20, 2008 support for claim 11, particularly sections c. and d. is found in paragraph 0017 of the patent publication, see Remarks page 9, 1st full paragraph. The Examiner has reviewed that section of the specification and notes CDP/Cux p110 isoform contains CR2,

CR3 and HD while the p75 isoform contains CR3 and HD. Applicants' claims are broader than what is supported in the specification. As the claims read any CDP/Cux isoform is missing Cut repeat domains, CR1 and CR2 and contains only two DNA binding domains. Furthermore, paragraph 0006 of the publication does cite CDP/Cux isoform, p75 is encoded by mRNA initiated within intron 20, however this is not the case for the three other three isoforms. However, the claims read broadly on all truncated CDP/Cux polypeptide variants having these characteristics. Applicants have not pointed out where in the specification support can be found for the wide breadth of the claims, as well as a method of detecting a level of an amino-terminally truncated CDP/Cux polypeptide variant wherein the polypeptide is a combination of the variants listed in sections a.-d. in claims 11 and 26.

Applicants assert support for claim 20 can be found in several paragraphs of the publication, see Remarks, page 10, 3rd paragraph. Claim 20 recites a method of detecting an amino-terminally truncated CDP/Cux polypeptide variant in combination with an additional CDP/Cux polypeptide, which may be a combination of isoforms, p200, p110, p100 or any combination of the said three isoforms. The specification does not disclose this claimed method of detection.

Claims 27 recites a kit wherein a detecting reagent is a second antibody conjugated to a combination of labels. The Examiner notes in paragraph 0042, page 5 of the publication secondary reagents for detection may be labeled with radioactive compounds, enzymes, biotin, or fluorochromes, but not a combination of these molecules.

Applicants are requested to delete the new matter or clearly and distinctly recite where in the specification support can be found for these new claims.

13. Claims 11-20 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In anticipation of the instantly claimed method Applicants assert the new claims recite variants with defined characteristics and the disclosure supports the genus covered by examined independent claims 11 and 26, see page 11, section 3.1 of Remarks submitted August 20, 2008. These points of view have been carefully considered, but found unpersuasive.

Applicants broadly claim a method for detecting a level of amino-terminally truncated CDP/Cux polypeptide variant in a sample wherein the polypeptide variant is:

a) a variant which is encoded by a nucleic acid produced from transcriptional initiation within intron 20 of the CDP/Cux locus;

b) a variant which is encoded by a CDP/Cux mRNA comprising a translation start site within exon 21;

c) a variant which lacks Cut repeat domains CR1 and CR2;

d) a variant which contains only two DNA binding domains; or

e) any combination of a)-d).

The written description in this instant case embraces unknown isoforms, as well as those yet to be identified and characterized. In the instant case, Applicants cite a variant of CDP/Cux polypeptide with only two DNA binding domains. There is no notation of which two binding domains must be retained in the variant and moreover the claims read on a combination of variants, hence the claims include a multitude of variants that may not have structure and function applicable to a method of detecting a level of an amino-terminally truncated CDP/Cux. It is not clear from the claims which amino acid residues are truncated from the CDP/Cux polypeptide variant, nor what amino acid residues define a fragment of a CDP/Cux polypeptide variant. Applicants' seem to be only in possession of human CDP/Cux isoforms, p200, p100, p110 and newly discovered p75. The written description is not commensurate in scope with the broadly claimed method encompassing a plethora of CDP/Cux isoforms yet to be discovered.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115). With the exception of human CDP/Cux isoforms listed herein, the skilled artisan cannot envision the detailed structure of the plethora of polypeptides labeled as CDP/Cux isoforms. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

At the time the application was filed, Applicants only had possession of the

human CDP/Cux isoforms, p200, p100, p110 and newly discovered p75. Moreover, the specification does not evidence the possession of all the possible polypeptides embraced by the term CDP/Cux polypeptide variant or fragment thereof, nor the entire genus of CDP/Cux isoforms as broadly claimed. There is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims does not meet the written description provision of 35 U.S.C. 112, first paragraph.

6. Claims 11-20 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting the presence or absence of CDP/Cux isoforms comprising contacting a sample with an antibody, which specifically recognizes a truncated CDP/Cux isoform, does not reasonably provide enablement for simultaneously detecting a combination of truncated CDP-Cux variants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants have set forth arguments asserting the newly presented claims recite a method of detecting a CDP/Cux variant for diagnosis of cancers found in breast tissue and blood, particularly acute myeloid leukemia (AML), see page 11 of the Remarks, section 3.2.

Applicants' claims read broadly on a method of detecting a level of an amino-terminally truncated CDP/Cux polypeptide variant or a combination of variants. Further dependent claims note the isoform is detected with an antibody, which specifically recognizes a truncated CDP/Cux. Applicants' specification notes detecting truncated isoforms of CDP/Cux isoforms such as p75, p100, p110 and p200 with an antibody.

It is art known that cancer broadly includes solid cancers, hematological cancers, benign cancers, as well as those types of cancer that are metastatic. Information on one cell type cannot be extrapolated to read on the same type of cell from a different organ system. Applicant's specification notes general methods of detecting truncated CDP/Cux isoforms, see pages 17-19 of the specification. Consequently, the specification seems to only support detection of truncated CDP/Cux isoforms in breast tissues, uterine tissues and acute myeloid leukemia (AML) cell lines, see specification, page 10, lines 28-31; page 18 and Moon (Int. J. Cancer 100: 429-432, August 2002). This information cannot be relied upon as enabling disclosure of a method of detecting breast cancer and AML with a combination of undefined and uncharacterized polypeptide variants. Based on what is known in the art the claims are not fully enabled. In view of the analysis set forth above there is insufficient guidance and a significant preponderance of unpredictability to one skilled in the art to implement the claimed method with a reasonable expectation of success. In view of the unpredictability of the art one of skill in the art would be forced into undue

experimentation to assess and glean what exactly is a result for the broadly claimed invention.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 11-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants aver in section 3.3 of the Remarks beginning on page 11 the claims now recite a complete method. However, the Examiner has reviewed the claim language and Applicants' response and they have been carefully considered, but found unpersuasive.

a. Claim 11 reads on a method for detecting a level of an amino-terminally truncated CDP/Cux polypeptide variant in a sample. However, the claims do not note how the isoform is detected, nor which isoform. This claim is vague and indefinite because if recites an incomplete method. The claims do not recite a *complete* method. Applicants must present the claim in clear, concise and definitive language for one of ordinary skill in the art to clearly distinguish what is being claimed. Applicants are requested to provide all the components required to detect the isoform in a sample and how this implemented. It is not clear what is the diagnostic tool used in the method or how the method is implemented without all the required active and positive steps delimiting how the use is actually practiced.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 11, 12, 14, 15 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Moon et al. (Molecular and Cellular Biology 21(18): 6332-6345, September 2001/ IDS reference C43 submitted April 5, 2006) as evidenced by Goulet (Biol. Chem. 387: 1285-1293, September 2006). Goulet notes the term CDP/Cux references both, the human and mouse gene and protein and the full length CDP/Cux protein, p200 contains three Cut repeats. Accordingly, Moon is prior art. Moon discloses the active step of detecting truncated CDP/Cut isoform in a sample, wherein nuclear extracts from untransfected 293 cells and transfected NIH 3T3 cells were analyzed in Western blots with CDP/Cut N-term, CDP/Cut 861, HA and Myc antibodies, see page 6334, Figure 2C. These antibodies recognized 200-kDA CDP/Cut protein, a 110-kDa protein, as well as 90 kDa protein, see page 6336, An amino-truncated…section.

11. Claims 11, 12, 14, 15 and 20 are rejected under 35 U.S.C. 102(a) as being anticipated by Moon et al. (Int. J. Cancer 100: 429-432, August 2002).

Moon discloses Western blot analysis comprising total protein extracts from uterine leiomyomas and matched normal tissue samples using α861 anti-CDP/Cux antibodies, see page 430. α861 anti-CDP/Cux antibodies recognize 3 isoforms, p200, p110 and p100, see Figure 1 on page 430.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 11, 12, 14, 15, 20, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moon et al. (Molecular and Cellular Biology 21(18): 6332-6345, September 2001/ IDS reference C43 submitted April 5, 2006). The teachings of Moon have been presented in the 102(b) rejection. Moon does not teach the disclosed method of detection comprised within a kit.

Although the claims recite a kit and a container for use, no positive recitation of the kit ingredients/elements distinguishes the claim over the reference. Therefore, the reference reads on the claimed kit and container of use. It is noted that kits traditionally include structural material such as instructions, labeling and promotional material. The container is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claim with the prior art. See MPEP 706.03(a). Thus the container

for use included in a kit or article of manufacture constitutes an "intended use" for that kit or article of manufacture. Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a kit containing an antibody that specifically recognizes a CCAAT-displacement protein/Cut homeobox isoform. One of ordinary skill in the art would have been motivated to make a kit because test kits including compounds are packaged for the advantages of convenience and economy for the ordinarily skilled artisan or the practitioner. Kits are conveniently made to reproducibly obtain results under test conditions and it is conventional to assemble necessary reagents including compounds, such as antibody conjugates for the effective treatment of cancer for the convenience of the practitioner and commercial expediency.

14. Claims 11, 12, 14, 15, 20, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moon et al. (Int. J. Cancer 100: 429-432, August 2002). The teachings of Moon have been presented in the 102(a) rejection. Moon does not teach the disclosed method of detection comprised within a kit.

Although the claims recite a kit and a container for use, no positive recitation of the kit ingredients/elements distinguishes the claim over the reference. Therefore, the reference reads on the claimed kit and container of use. It is noted that kits traditionally include structural material such as instructions, labeling and promotional material. The container is viewed as a

recitation of intended use and therefore is not given patentable weight in comparing the claim with the prior art. See MPEP 706.03(a). Thus the container for use included in a kit or article of manufacture constitutes an "intended use" for that kit or article of manufacture. Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a kit containing an antibody that specifically recognizes a CCAAT-displacement protein/Cut homeobox isoform. One of ordinary skill in the art would have been motivated to make a kit because test kits including compounds are packaged for the advantages of convenience and economy for the ordinarily skilled artisan or the practitioner. Kits are conveniently made to reproducibly obtain results under test conditions and it is conventional to assemble necessary reagents including compounds, such as antibody conjugates for the effective treatment of cancer for the convenience of the practitioner and commercial expediency.

15. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached on 7:30 am to 6:30 pm, Monday through Saturday with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The

fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
24 November 2008
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643